Allergy Abstracts

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From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 14, Number 5 September, 1949

Asthma and Hay Fever

Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm. III. Anticholinergic Agents. Beaky, J. F., Bresnick, E., Levinson, L., and Segal, M. S.: Ann. Allergy **7**: 113, 1949.

The protective action of certain anticholinergic drugs against the bronchospasm induced by mecholyl and histamine was studied in asthmatic patients. Protection was measured by the decrease in vital capacity produced by histamine or acetyl-beta-methylcholine before and after the administration of the therapeutic agent. Atropine in a dose of 0.6 mg. administered intravenously completely protected susceptible individuals against the effects of subsequent doses of intravenous mecholyl for two hours and afforded significant protection for an additional two hours. Intravenously administered Bellafoline in dosages of 0.5 mg. afforded complete protection against mecholyl for three hours and significant protection for a similar period. Although Bellafoline as an aerosol protected against aerosolized mecholyl for almost two hours, the protection time was doubled when the drug was administered intravenously. Scopolamine in subcutaneous doses of 0.3 mg. afforded complete protection against intravenously administered mecholyl for two hours and significant protection for another three. Orally administered scopolamine in dosage of 0.6 mg. offered significant protection against intravenous mecholyl for almost five hours after a latent period of one hour. Aerosolized scopolamine had a shorter protective action than when administered by other routes. None of the drugs studied protected against the bronchospasm of histamine. W.

Respiratory Air Flow Patterns in Children. Kaye, R., Whittenberger, J. L., and Silverman, L.: Am. J. Dis. Child. **77**: 625, 1949.

An air flow recorder which consists of a face mask with a wire mesh diaphragm is described. Slight variations in pressure occurring within the mask are magnified and recorded on photographic film by a pneumotachograph. The subject is unaware of any obstruction to breathing and hence the study of infants and children is facilitated.

Respiratory patterns of normal infants, children, and adults were recorded. Asthmatic children studied during attacks produced a typical abnormal pattern. "They all show rapidly attained and poorly maintained expiratory air flow, i.e., decline in velocity shortly after peak flow is reached, loss of the oscillations which are normally superimposed on the basic variations, and a high degree of uniformity in the pattern of successive respiratory cycles." Other asthmatics examined between attacks showed normal tracings. Adults with pulmonary complications of asthma, such as emphysema, may show abnormal tracings in the absence of active asthma. Other pulmonary conditions which produced abnormal tracings were bronchiectasis, kyphoscoliosis, and the pulmonary disease associated with fibrosis of the pancreas. K.

Bronchoscopic Observations on the Pulmonary Aspects of Fibrocystic Disease of the Pancreas. Atkins, J. P.: Ann. Otol., Rhin. & Laryng.: **57**: 791, 1948.

Local and systemic factors contribute to the mechanism involved in bronchopulmonary infections of the allergic patient. The fundamental systemic defect of altered reactivity to the allergen is expressed in the lung as bronchial asthma. Similarly, the importance of a systemic disturbance must also be recognized in the chronic pulmonary infections associated with fibrocystic disease of the pancreas. The bronchoscopic findings in this condition are sufficiently characteristic to suggest the diagnosis. The picture is that of a hyperemic, sometimes granular, mucosa with thickening of the bronchial spurs. The lumen is obscured by the presence of extremely viscid, purulent mucus. When this is aspirated the hyperemic bronchus shows marked expiratory intrusion of the posterior wall into the lumen, producing a bronchus with a crescentic cross section resembling that seen in the asthmatic patient. This disease must be considered in the differential diagnosis of the chronic pulmonary infections of childhood. C.

Bronchopulmonary Infections in Allergic Individuals. Davison, F. W.: Ann. Otol., Rhin. & Laryng.: **57**: 884, 1948.

A review of hospital charts of one hundred unselected cases who had undergone bronchoscopic examinations revealed that forty-nine patients were atopic. Of these, twenty had bronchiectasis, fifteen had chronic bronchitis, ten had asthma and chronic bronchitis, and four had allergic pulmonary consolidation. Seventy-six per cent of the patients with bronchiectasis were allergic and fifteen of the forty-nine atopic individuals had chronic bronchitis. The high incidence of allergy in bronchiectasis and chronic bronchitis emphasizes the importance of allergic management in the treatment of these bronchopulmonary infections. C.

A Comparative Study of Commercial Nebulizers. Harsh, G. F.: Ann. Allergy **6**: 535, 1948.

The effectiveness of the various types of nebulizers commonly used for inhalation therapy is discussed. The amount of solution delivered by one compression of the hand bulb varied widely in different models. Not only the quantity of solution delivered, but also the size of the droplets emitted must be considered. Thus, in conditions where it is desirable to have the medicant pass far down the bronchial tree, a nebulizer should be used which produces a spray of fine particles. The author discusses the advantages of adding glycerin to adrenalin mixtures in the treatment of asthmatics. It is concluded that no nebulizer is ideal for all purposes. R. WISEMAN.

Breathing Exercises as an Adjunct in the Treatment of Bronchial Asthma and Pulmonary Emphysema. Dorenson, S. M.: Am. Pract. **3**: 550, 1949.

Breathing exercises designed for asthmatic and emphysematous patients are outlined and illustrated. Fifty-two patients with bronchial asthma and/or emphysema, ranging in age from 5 to 72 years, were trained in the proper methods of breathing by means of these exercises. Subjectively, the majority of the patients experienced moderation of their attacks and in some instances developed the ability to abort them. Objectively, there was an increase in exercise tolerance and vital capacity. F.

Dermatology

Dermatitis Venenata From Organomercurial Compounds. Gaul, L. E., and Underwood, G. B.: J. A. M. A. **140**: 861, 1949.

Organomercurial compounds applied to the intact skin are relatively poor sensitizers. When employed as surgical antiseptics, however, they may induce sensitivity as manifested by dermatitis resembling stitch abscess, wound disruption, or infection and delayed healing. When cutaneous protective barriers are disrupted, a higher incidence of acquired sensitivity occurs. These reactions may occur within one day of application or several weeks later. As the duration of application is prolonged, the likelihood of sensitization increases. The appearance of pustules in or around a wound may be a sign of sensitization usually detectable by a positive patch reaction. Another sign of mercurial sensitivity is a disruption of a healing wound. A vesicular eczema may appear and spread rapidly. The morphologic character of the sensitization reaction may vary markedly. When pustular, it may frequently be confused with infection, and further treatment with mercurials results in intensification of the dermatitis and often a generalized rash. Reactions to the organomercurials are highly specific. There is a tendency to group reactions among them. The ingestion of inorganic mercurials, such as calomel in the presence of cutaneous sensitivity to ammoniated mercury, may produce severe generalized urticarial dermatitis. It is suggested that patients should be patch tested before any of the mercurial diuretics are administered in order to avoid the possibility of severe or even fatal systemic reactions. F.

A Case of Sensitivity to Gold-Ball Orbital Implant. Forster, Jr., H. W., and Dickey, R. F.: Am. J. Ophth. **32**: 659, 1949.

Following enucleation of an eye, a 14-carat gold ball was implanted into Tenon's capsule in a 29-year-old woman. Five years later, a purulent discharge from the orbit developed, accompanied by a contact type of dermatitis

involving the eyelids and the adjoining malar region. This condition failed to respond to all types of therapy. Sensitivity to the gold was suspected and patch tests were performed with the metallic components of 14-carat gold. Strongly positive reactions were obtained only to the pure gold leaf. A patch test with the gold ball itself was strongly positive and was accompanied by a generalized urticaria. The test was repeated on the opposite arm three days later with the same results. Following the removal of the gold ball all lesions disappeared. C.

An Evaluation of Therapy in Infantile Eczema. Hill, L. W.: J. A. M. A. **140**: 139, 1949.

Under the general term, infantile eczema, are included such different dermatoses as nummular eczema, the atopic, contact, and seborrheic dermatitides, and fungus infections. The atopic and contact types are based on allergy. Many cases of atopic infantile eczema show positive cutaneous reactions of the urticarial type, but these reactions are not always of clinical significance. Many of them indicate only a subclinical sensitivity. Very young infants with atopic dermatitis usually show positive scratch reactions to milk, egg, and wheat. Inasmuch as they eat no egg, this food may play no part in the causation of the eczema, but the marked reactions to milk and wheat are usually of clinical importance. To determine whether a food is a causative factor, it must be eliminated from the diet, but care must be taken to maintain an adequate food intake. Goat's milk, as a substitute for cow's milk, is seldom as satisfactory as soybean products, but neither should be used unless a positive skin reaction to milk has been elicited. Many cases of infantile eczema are unrelated to diet and frequently they are the result of contact sensitivity. The time of onset, distribution of the lesions, and patch tests may be helpful in making this diagnosis. Local therapy is important in all types of infantile eczema and should include the use of bandages to serve as a protection against scratching. In the author's experience, the antihistaminic drugs have been of little value in allaying pruritus. The use of unsaturated fatty acids has also proved disappointing, but needs further investigation. F.

Professional Streptomycin Hypersensitivities Among Hospital Staffs. Marcussen, P. V.: Acta dermat.-venereol. **29**: 411, 1949.

Systematic patch testing of 143 nurses handling streptomycin in three different hospitals revealed twenty cases of eczematous hypersensitivity to streptomycin. A definite relationship between the degree of exposure and the development of hypersensitiveness could be established. One nurse developed a violent eruption when she received an intramuscular injection of hormone from a syringe previously used for streptomycin therapy. Careful instructions to personnel for avoidance of contact with streptomycin are advised. H.

Palpebral Eczema Due to Streptomycin. Dufour, R.: Praxis **37**: 427, 1948.

Four of five nurses handling streptomycin developed acute palpebral eczema and one developed a chronic blepharoconjunctivitis. Two in the group also had eczema of the fingers. Strongly positive reactions to patch tests were noted in all cases. Seven other nurses handling the drug were not affected. Sensitization appeared after three to twelve months of contact. Streptomycin appears to be a strong eczematogenic agent. H.

House Ivy Dermatitis. Rynes, S.: Ann. Allergy **7**: 62, 1949.

A case of recurrent summer dermatitis with a positive patch test to house ivy is described. Following a course of injections with an alcoholic extract of ivy leaves, the skin remained clear during the summer for the first time in many years. R. WISEMAN.

Otorhinology and Ophthalmology

Intranasal Medication With Vasoconstrictors. Van Alyea, O. E., and Donnelly, A.: Trans. Chicago Laryng. and Otol. Soc. In Arch. Otolaryng. **49**: 234, 1949.

The effects of the use of nasal vasoconstrictors were studied on eleven patients with hypertension, sixteen with cardiac disorders, nine with thyroid disturbances, and fourteen with diabetes. Five drops of Neo-Synephrine hydrochloride (phenylephrine hydrochloride N.N.R.) in strengths of 1 per cent and 0.25 per cent were instilled into each nostril with the patient in the lead-low position. After several minutes, the patient was returned to the sitting position and pulse and blood pressure readings were made at intervals for forty-five minutes. No untoward effects were noted. C.

Use of Antihistaminic Drugs in Control of Atropine Dermatitis and Conjunctivitis. Fralick, F. B., and Kress, R. D.: Arch. Ophth. **41**: 583, 1949.

A contact dermatitis and conjunctivitis occasionally develops in patients using atropine in treatment of iridocyclitis, necessitating discontinuance of the drug. It is difficult to find a substitute for atropine since the patient who is sensitized to it tends also to be sensitive to similar drugs such as homatropine, scopolamine, or duboisine. In nine cases of atropine dermatitis and conjunctivitis, the authors were able to continue atropine therapy by the administration of antihistaminics. The treatment of choice was a combination of oral administration of tripelennamine hydrochloride and local use of diphenhydramine hydrochloride. C.

Miscellaneous Allergies

On Allergy to Cottonseed Oil. Bernton, H. S., Coulson, E. J., and Stevens, H.: J. A. M. A. **140**: 869, 1949.

Two patients with positive cutaneous reactions to the water-soluble cottonseed antigen were studied in an effort to determine whether they were clinically sensitive to cottonseed oil. The first patient stated that ingestion of cottonseed oil never provoked symptoms. The second patient (a physician) maintained that contact with nonabsorbent cotton or sleeping on a cotton-filled mattress produced hives and that the ingestion of cottonseed oil precipitated gastrointestinal symptoms. Passive transfer studies made with the serum of the first patient resulted in positive reactions by direct test or by ingestion of the water-soluble antigen, but negative reactions were obtained with the oil. The serum of the physician, who thought that he was clinically sensitive to the oil did not contain reagins to either the water-soluble antigen or to cottonseed oil. When he was fed large doses of unlabelled cottonseed oil, he could not distinguish between this and other oils. These findings confirm previous evidence that specific sensitiveness to water-soluble allergic extracts of defatted cottonseed (embryo) does not imply clinical sensitivity to edible cottonseed oil.

Drug Allergy. Sherman, W. B.: J. A. M. A. **140**: 447, 1949.

Studies of histologic lesions of drug hypersensitivity may show characteristic changes by which drug allergy may be distinguished from toxic reactions. Chief among these pathologic findings are arteritis with localized fibrinoid and hyaline degeneration of the media and perivascular infiltration and focal necrosis with mononuclear infiltration of the myocardium, spleen, liver, and other organs. Reactions from drugs may be severe and even fatal. Cutaneous tests are of no value in determining sensitivity to crystalloid drugs, but may be diagnostic in sensitivity to protein drugs and vegetable gums. Gums which are used as excipients or cohesive agents in the preparation of many pills, may be the cause of a hypersensitivity reaction which is erroneously attributed to the drug.

Drug fever is an indication of sensitivity which usually precludes further use of the offending or closely related drugs. Drug fever should not be confused with an infectious process. Drug rashes vary widely and are the most common manifestation of drug allergy. Once the skin has become sensitized, subsequent use of the drug, either orally or topically, may cause a prompt reaction. In a considerable number of patients, contact sensitization may be accompanied by a generalized sensitivity.

Jaundice may be the result of a toxic action, but in some cases it is due to hypersensitivity. It is usually of the obstructive type. When a drug is given in an interrupted course, jaundice is more frequent in the second course and after one attack further use of the drug is likely to cause a recurrence.

Agranulocytosis and thrombopenic purpura may also be manifestations of drug allergy and may occur suddenly in patients who have previously tolerated a drug for weeks or even months. Positive skin tests obtained with mixtures of drugs with human serum have been reported. F.

Tuberculin Allergy and the Sedimentation Rate of Red Cells in Human Tuberculosis Treated With Streptomycin. Zini, F.: Acta med. Scandinav. **133**: 145, 1949.

In twenty-three of twenty-seven patients with pulmonary tuberculosis, the sedimentation rate decreased following treatment with streptomycin. Changes were also noted in the skin reaction to crude tuberculin. Five patients, who had negative reactions to tuberculin, reacted intensely to the 1:100 solution following streptomycin treatment. Two cases with hyperergic reactions at the onset of the treatment showed little change. Of twenty patients with mild allergic responses to tuberculin, thirteen showed increased reactions to 1:1000 following treatment, six showed little change, and one showed a slight reduction in tuberculin sensitivity. H.

Treatment of Pernicious Anemia With Special Reference to Hypersensitivity to Liver Extract. Malmros, H., and Herner, B.: Nord. Med. **40**: 2133, 1948.

Seventeen cases of pernicious anemia with sensitivity to liver extract were treated perorally with a maintenance dose of folic acid and a stomach-liver preparation daily. The results were satisfactory in fifteen cases. Two patients who developed neurological symptoms were desensitized with liver extract and, subsequently, treatment was resumed. The neurologic symptoms disappeared when liver therapy was instituted. Folic acid is potentially dangerous because of the possibility of the occurrence of neurologic complications. Constant examinations for the detection of neurologic complications are essential in patients on folic acid therapy. H.

Loeffler's Syndrome and Pulmonary Infiltrations Accompanied by Peripheral Eosinophilia. Ham, J. C., and Zimdahl, W. T.: Ann. Int. Med. **29**: 488, 1948.

Three cases of pulmonary infiltration with blood eosinophilia are reported. In the first patient the unusually long, stormy course was accompanied by minimal physical findings as compared to the x-ray findings. The blood eosinophilia was 41 per cent. Excellent relief was obtained with intravenous Aminophyllin. The personal history was negative for allergy, but the family history was positive. In the second case the course was less severe but protracted, and the onset was suggestive of angina pectoris. The third patient, who gave a history of hay fever, had two episodes of pulmonary infiltration and eosinophilia. The etiological agent was not discovered in any of the cases. A plea is made for a more useful and standard nomenclature for these cases since there has been a tendency to associate Loeffler's syndrome with any case of pulmonary infiltration and eosinophilia. H.

Loeffler's Syndrome—Periarteritis Nodosa. Tomenius, J.: Acta med. Scandinav. **133**: 55, 1949.

Two cases of periarteritis nodosa preceded by typical signs of Loeffler's syndrome are presented. One case, first diagnosed as eosinophilia leucemoides (Engbach), was found to be periarteritis nodosa at postmortem. The diagnosis of periarteritis nodosa was made by muscle biopsy in the second case. The author believes that the cases previously described by Engbach were periarteritis nodosa with a leucemic reaction. The suggestion is made that biopsy of the pectoral muscle be done in all cases of Loeffler's. H.

Anaphylaxis

The Release of Histamine and Heparin by Antigen From the Isolated Perfused Liver of the Sensitized Dog. Scoggie, A., and Jaques, L.: J. Immunol. **62**: 103, 1949.

Horse serum was found to be a more potent antigen than egg white in sensitizing dogs. In moderate or severe shock there was a significant increase in the blood levels of both histamine and heparin and a decrease in the number of circulating platelets. Perfusion of the isolated liver with either of the antigens did not result in any release of histamine or heparin. However, perfusion of the liver in situ with antigen produced a marked release of histamine and heparin in two out of six animals.

Using a modified method, isolated liver was again perfused with antigen. In three experiments where the antigen was injected with Tyrode's solution and then fifteen minutes later perfused with blood, no anaphylotoxins were released. However, when the livers were perfused with horse serum in silicone blood, a majority of the animals showed an increase in blood histamine and heparin. In more sensitive animals whose liver blood was flushed out with Tyrode's solution, a release of histamine and heparin was obtained after the animals were challenged with antigen in Tyrode's solution, indicating that the reaction in the liver did not depend on any blood constituent. Since it was found that in animals not so highly sensitized, the release of histamine and heparin was more likely to occur when blood was used as the perfusing medium, it may be concluded that blood, although not absolutely essential to the anaphylactic reaction, in some way aids that reaction. The suggestion is made that blood owes this superiority to its ability to maintain the liver

cells in good physiological condition for the reactions leading to the release of histamine and heparin after the union of antigen and antibody has occurred in these cells. Although platelets had been indicated as an etiological factor in the mechanism of shock, the fact that blood was not a necessary constituent for the reactions tends to disprove this theory. R. WISEMAN.

An Investigation Into the Presence of Antibodies and Hypersensitivity in the Encephalitis Produced Experimentally by the Injection of Homologous Brain Suspensions. Hill, K. R.: Bull. Johns Hopkins Hosp. **84**: 302, 1949.

Encephalitis was produced in a majority of guinea pigs injected subcutaneously with a saline suspension of either fresh, phenolized, or heated homologous brain tissue emulsified with a water-in-oil suspension of killed tubercle bacilli and Falba. Most of the animals exhibiting neurological signs showed histologic evidence of brain lesions. The principal reaction appeared to be a vascular and perivascular inflammation varying from an acute to a subacute stage. The lesions were entirely localized to the central nervous system. Monocytes were the predominating infiltrating cells, but polymorphonuclears were present in large numbers. Eosinophiles were rarely found. There was an apparent demyelinization in the narrow zone around vessels acutely affected, but not in the interstitial tissues. The meningeal infiltrates were almost entirely mononuclear. The choroid plexus and cerebellum were frequently affected. About one-half of the injected guinea pigs developed specific complement fixing antibrain antibodies in their sera. However, there was no correlation between the appearance of paralysis or histological lesions and the presence of these antibodies. Flocculating antibodies were not found in guinea pig sera.

Encephalitis could not be produced in rabbits by the same technique. All injected rabbits gave specific complement fixing and flocculating antibrain antibodies. All rabbit sera, including controls and normals, contained "natural" complement fixing antibodies for saline-brain suspension antigen. Attempts to produce encephalitis in normal animals by passive transfer of serum, peritoneal washings, splenic or lymph node tissue from affected animals all failed. Skin tests with brain tissue on all test animals were negative. Attempts to elicit the Prausnitz-Küstner reaction also failed. No relationship between the meningoencephalitis and the presence of antibrain antibodies could be demonstrated in these studies. B. SIEGEL.

Tissue Culture Studies on Liver Cells of Anaphylactically (Arthus) Sensitized Animals in the Presence of the Sensitizing Antigen. Buckley, J. J., Buckley, S. M., and Gey, M. K.: Bull. Johns Hopkins Hosp. **84**: 195, 1949.

Adult albino rabbits were given repeated subcutaneous injections of horse serum until an intracutaneous injection of the antigen produced an Arthus reaction with necrosis. Liver tissues from sensitized and control rabbits were then cultured in several types of media and studied microscopically. There was no qualitative or quantitative difference between the growth or appearance or duration of viability of the liver cells of normal and of hypersensitive rabbits, whether in the presence or absence of specific antigen or antibody. It is suggested that the focal necrosis which occurs in the liver of the anaphylactically sensitized animals following the intravascular injection of the antigen may be due to vascular alteration, rather than to direct action of the antigen upon the epithelial liver cells. B. SIEGEL.

Separation by Means of Ammonium Salts of the Antibody-Antigen Reaction From the Response of the Smooth Muscle. Weil, A. J., and Rose, E.: Ann. Allergy **7**: 109, 1949.

Ammonium salts in concentrations of $\frac{1}{40}$ to $\frac{1}{10}$ molarity inhibited the histamine contractions of guinea pig ileum strips in the Dale bath. After these strips were repeatedly washed, normal muscular contractions were again obtained on the addition of histamine to the bath. Slightly higher concentrations of ammonium salts similarly antagonized acetylcholine. The contraction of sensitized strips which was induced by homologous antigen was inhibited by ammonium salts in the same concentrations that were effective in histamine and acetylcholine experiments. However, this inhibitory action did not affect the combination of antigen and antibody. W.

A Quantitative Study of Passive Anaphylaxis in the Guinea Pig. IV. Passive Sensitization With Non-Precipitable or "Univalent" Rabbit Antiovalbumin. Kabat, E. A., and Benacerraf, B.: J. Immunol. **62**: 97, 1949.

Samples of rabbit antiovalbumin sera were serially absorbed with antigen until they were found to be free of precipitable antibody. The amount of nonprecipitable (univalent) antibody in the aliquot portions was determined. Further addition of antigen completely neutralized the "univalent" antibody. Guinea pigs were sensitized intravenously with fractions of the antiovalbumin sera containing varying amounts of precipitable and nonprecipitable antibody. After forty-eight hours, the animals were shocked intravenously with equal amounts of antigen. On a weight basis, as measured by nitrogen content, the sensitizing capacity of the "univalent" antibody was equal to that of the usual heterogenous mixture of antibodies in the original serum. This sensitizing power was lost when excess antigen was present. These findings explain the capacity of certain antisera to induce passive anaphylactic sensitization in the absence of detectable precipitins. It is suggested that in the presence of enough antibody molecules, "Anaphylaxis can be initiated without the formation of a huge aggregate of antigen and antibody molecules and, indeed, by the reaction of not more than one molecule of antigen for each molecule of antibody." B. SIEGEL.

Active Constriction of Hepatic Venous Tree in Anaphylactic Shock. Relation to Centrilobular Lesions. Macgraith, B. G., Andrews, W. H. H., and Wenyon, C. E. M.: Lancet **257**: 56, 1949.

Dogs, rats, and guinea pigs were sensitized by repeated intravenous injections of horse serum. After an adequate incubation period the liver was exposed and the antigen was injected just below the surface. Within a few minutes a well-defined area of congestion exhibiting a "lobular" pattern appeared. Histologically, the congestion was predominantly centrilobular. The same site was refractory to a second injection. When larger quantities of antigen were injected into a branch of the portal vein supplying a lobe, congestion of the whole lobe resulted. When still greater quantities were injected intravenously, congestion of the whole liver was noted. These reactions occurred with less regularity in rats and guinea pigs, and could not be produced in rabbits. Those animals which did not develop a local hepatic reaction also failed to show generalized reactions when the antigen was given intravenously. Similar hepatic reactions could be produced in animals sensitized with injections of minute amounts of horse serum directly into exposed livers. It is believed that the primary reaction is a constriction of both small and large radicles of the hepatic veins causing centrilobular congestion and stagnant anoxia. When the congestion is unrelieved, degenerative and necrotic cellular changes occur. B. SIEGEL.

Experimental Anaphylactic Iridocyclitis. Foss, B.: Acta path. et microbiol. Scandinav. 1949, Suppl. 81 (128 pages).

The injection of 0.1 ml. of foreign serum or egg albumin into the vitreous of the eye in albino rabbits results in an iridocyclitis after a definite incubation period. This reaction has been termed "primary anaphylactic iridocyclitis." If the foreign serum is injected together with a cellular poison, there is an immediate toxic reaction followed by an anaphylactic reaction after the necessary incubation period.

Rabbits, sensitized, generally develop an immeditae iridocyclitis following the injection of homologous antigen into the vitreous. Rabbits that have had a primary reaction will develop a specific "secondary anaphylactic iridocyclitis" following the intravenous or subcutaneous injection of homologous antigen. This reaction occurs within a few hours if the antigen is given intravenously and within twenty-four hours if given subcutaneously. The presence of horse serum could be demonstrated in the blood of nonsensitized rabbits up to the fourth day following the injection of 0.1 ml. of horse serum into the vitreous. Precipitins for horse serum could be detected in these animals on the sixth or seventh day in a dilution of 1:100,000. The formation of antibodies which followed the intravitreous administration of 0.1 ml. of horse serum or egg albumin was greater than that which followed the intracutaneous injection of the same amounts of antigen. H.

Immunological Studies on Egg White Protein. Cohn, M., Wetter, L. R., and Deutsch, H. F.: J. Immunol. **61**: 283, 1949.

The precipitin reactions produced by highly purified conalbumin and six times recrystallized ovalbumin with their homologous horse- and rabbit-antisera were studied. In most cases protein impurities in a given preparation were found to be antigenic. Though conalbumin, in the electrophoretic apparatus, moved in a single boundary in the pH range of from 3.0 to 8.6 and was homogeneous in the ultracentrifuge, it was definitely inhomogeneous by immunological criteria. Although ovalbumin showed two components electrophoretically, these were indistinguishable immunologically. In interpreting quantitative precipitin curves, the authors found that the antibody response to any impurity or minor component in a protein preparation may be greater than to the main component itself. They stress the necessity of carrying the curve far into the region of antigen excess in order to demonstrate more than one immunologically active component, either in the antigen or antiserum. R. WISEMAN.

Hypersensitivity in Cold-Blooded Animals. II. Salamanders. King, J. W., and Dreyer, N. B.: Science **109**: 568, 1949.

American newts *(Triturus viridescens)* injected intraperitoneally with horse serum and shocked 18 to 55 days later showed no evidence of hypersensitivity. The injection of 5 gamma of histamine phosphate produced no effect, but 10 gamma produced a transitory reaction of obvious distress which was considered to be artifact. Intestinal strips of these animals did not respond to histamine (10 gamma), epinephrine (10 gamma), or horse serum (0.2 ml), but contracted on stimulation with barium chloride (2 per cent solution).

Mudpuppies *(Necturus maculosus)* injected in the same manner did not react to shocking doses of antigen. Stomach, intestine, and "Straub heart" preparations of these and of normal animals failed to respond to histamine (10 gamma) and horse serum. Myocardial contractions were increased by epinephrine (1 gamma) and depressed by acetylcholine (1 gamma).

The findings in salamanders were unlike those in teleost fish, which can be sensitized to protein antigens and show histamine shock as well as smooth muscular contraction in vitro to histamine. I. GLAZER.

The Effect of Lithium Periodate on Crystalline Bovine Serum Albumin. Goebel, W. F., and Perlman, G. E.: J. Exper. Med. **89**: 479, 1949.

Crystalline bovine serum albumin was oxidized with lithium periodate. The resulting denatured product retained many physical and chemical properties of protein but was incapable of eliciting antibodies in rabbits. However, antibodies to undenatured bovine albumin specifically precipitated the denatured product. K.

Pharmacology, Physiology, and Pathology

Lymphopenia and the Secretion of Adrenalin. Gellhorn, E., and Frank, S.: Proc. Soc. Exper. Biol. & Med. **71**: 112, 1949.

Adrenodemedullated fasting rats reacted with a marked lymphopenia to intraperitoneal injection of adrenalin. Sixty minutes following hemorrhage, lymphocytes in normal rats fell to 67 per cent of the control value as compared to 92 per cent in adrenodemedullated animals. The almost constant red count indicated that the differences were not due to dilution of the blood but to a reaction dependent on the secretion of adrenalin. A similar lymphopenia was obtained in normal rats after a "rage" induced by a subconvulsive electrical shock.

Insulin hypoglycemia in normal rats produced lymphopenia. The lymphopenia in adrenodemedullated animals was less marked. The data suggested that in hypoglycemia the increased secretion of adrenalin contributed to the lymphopenia. However, adrenalectomized rats in insulin coma also showed a fall in lymphocytes but less than those in demedullated rats and no characteristic change in neutrophils. This suggested that in addition to the lymphopenia initiated by the secretion of adrenalin, some other effect of low blood sugar on the adrenal cortex occurred which lead to lymphopenia independent of changes in the secretion of adrenalin. I. GLAZER.

Effect of Cortical Extract and Other Agents on Eosinophilia of Mice Infected With Trichina Spiralis. Stein, K.: Proc. Soc. Exper. Biol. & Med. **71**: 225, 1949.

When young adult mice were fed pectoral muscle from trichinous hosts, an eosinophilia was produced which lasted for at least five weeks. Adrenal cortical extract and adrenalin both caused a marked fall in the absolute number and in the percentage of circulating eosinophils. However, in adrenalectomized animals, adrenalin produced no effect. Sex steroids did not significantly reduce the number of circulating eosinophiles in four intact and two adrenalectomized animals. Urethane also caused an eosinophilia but the author was unable to determine whether the adrenal cortex was necessary for this action. R. WISEMAN.

Minimal Effective Dose of Intravenously Administered Histamine in Pregnant and Non-Pregnant Human Beings. Janowitz, H., Grossman, M. I.: Am. J. Physiol. **157**: 94, 1949.

Histamine was administered intravenously to a series of thirty-six adults. The group included twelve normal males, fourteen nonpregnant females, and ten females in the second and third trimesters of pregnancy. In twenty-five per cent of these subjects, two to four micrograms of histamine base was the minimal effective dose for the production of facial and cerebral blood vessel changes and stimulation of the taste receptors. It required ten micrograms to effect these changes in the remaining seventy-five per cent of the subjects. Despite the reported increase of serum histaminase during pregnancy, the range of minimal effective doses of histamine given rapidly into the vein was the same for pregnant and nonpregnant subjects. F.

Histamine-Sympathin Balance. Farrerons-Co., F. J.: Ann. Allergy **7**: 46, 1949.

Sympathin was obtained by extracting the spleen, heart, and liver of freshly killed dogs and calves. When this crude extract was injected into dogs, the histamine content of the blood rose concomitantly with the blood pressure. Conversely, pressor substances, which caused a reduction in blood pressure, produced a fall in blood histamine content. Sympathin, added to the Dale bath, inhibited the response of guinea-pig ileum strips to subsequent stimulation with histamine. It also protected up to 60 per cent of guinea pigs and over 80 per cent of rabbits against the shock of histamine administered parenterally. Seventy-nine per cent of guinea pigs receiving Sympathin were protected against histamine aerosol. This protection was long lasting. Three out of four rabbits pretreated with Sympathin survived as many as three lethal doses of histamine administered twelve days later. W.

The Hyperglycemic Action of Some Analogs of Epinephrine. McChesney, E. W., McAuliff, J. P., and Blumberg, H.: Proc. Soc. Exper. Biol. & Med. **71**: 220, 1949.

Epinephrine analogs were injected subcutaneously into healthy adult rabbits with a fasting blood sugar below 130 mg. per cent. Venous blood samples were taken at one, two, three, and five hours after the injection. The approximate hyperglycemic activities of the compounds studied, expressed in percentage of the hyperglycemic activity of l-epinephrine were: l-arterenol, 12 per cent; Win 3046, 1.7 per cent; Butanefrine, 1.6 per cent; Win 515, 0.7 per cent; d-arterenol, 0.6 per cent; and Isuprel, 0.12 per cent.

H. Glazer.

Veratramine, an Antagonist to the Cardioaccelerator Action of Epinephrine. Krayer, O.: Proc. Soc. Exper. Biol. & Med. **70**: 631, 1949.

The heart rate of a dog heart-lung preparation was kept between 200 to 260 per minute by continuous infusion of 0.33 to 0.65 c.c. of epinephrine 1:100,000 per minute. One milligram of veratramine promptly reduced the rate to or near the normal without change in the regular sinus rhythm. The veratramine effect which lasted for one hour could be overcome at least partially by high concentrations of epinephrine. Atropine did not abolish the effect. After pretreatment with veratramine, experimental heart failure could be relieved by epinephrine without cardioacceleration. Jervine, another veratrum alkaloid, had a similar effect. It was thus possible to separate the positive chronotropic from the positive inotropic effect of epinephrine.

I. Glazer.

Effect of Tagathen on Histamine-Induced Gastric Lesions in Guinea Pigs. Van Meter, J. C., and Oleson, J. J.: Proc. Soc. Exper. Biol. & Med. **71**: 163, 1949.

Gastric hemorrhages, erosions, and perforations were produced in 92 per cent of guinea pigs, on a synthetic diet, by intramuscular injections of 0.6 mg. histamine diphosphate twice daily. Similar results were obtained in animals on the basal diet plus kale ad libitum. Addition or omission of ascorbic acid did not have an appreciable influence. Out of ninety-two guinea pigs receiving 4 or more mg. of the antihistaminic Tagathen (N,N-dimethyl-N′-(2-pyridyl)-N′-(5-chloro-2-thenyl)-ethylene-diamine citrate), only 36 exhibited gastric lesions and a considerable number of these were minimal. With a higher dosage of Tagathen the incidence of gastric damage was further reduced. I. GLAZER.

The Prevention and Treatment of Motion Sickness. Gray L., and Carliner P.: Bull. Johns Hopkins Hosp. **84**: 5, 1949.

While Dramamine was being tested as an antihistaminic, its beneficial effects on the symptoms of motion sickness were discovered. It was further tested on a large number of soldiers who were crossing the Atlantic on an army transport in stormy weather. Placebos were used as controls. The drug was used on several hundred subjects and proved dramatically effective both in the prevention and treatment of seasickness. The incidence of toxic manifestations was minimal and in no instance was it necessary to discontinue the drug because of a reaction. The optimal dose was 100 mg. before meals and at bedtime. If patients were too sick to take the drug orally, excellent results could be obtained by rectal administration. R. WISEMAN.

Correlation of Experimental Data With Clinical Behavior of Synthetic Antihistaminic Drugs. Friedlaender, A. S., and Friedlaender, S.: Ann. Allergy **7**: 83, 1949.

Comparative studies of the clinical and experimental efficiency of Benadryl, Pyribenzamine, Antistine, Neoantergan, Neohetramine, and Thenylene were made. As a protective agent against fatal histamine shock in guinea pigs, Neoantergan was by far the most effective with Pyribenzamine, Thenylene, Benadryl, and Antistine following in that order. In anaphylactic experiments in guinea pigs in which the drugs were compared in pairs, Benadryl and Pyribenzamine afforded equal protection, Thenylene was more effective than Neohetramine, and Neoantergan was far superior to Antistine. In whealing studies in human subjects, Neoantergan was the most effective histamine antagonist, Thenylene, Pyribenzamine, and Benadryl were next in order, and Neohetramine and Antistine were least effective. The most satisfactory dosage in human subjects was 50 mg. for all drugs except Antistine and Neohetramine, of which 100 mg. was required. Neohetramine produced the least side reactions (12.14 per cent). Pyribenzamine, Neoantergan, and Thenylene afforded satisfactory symptomatic relief in most patients but some obtained more relief with the other drugs. In general the differences noted in the clinical studies were not as clear-cut as those noted in the experimental work. W.

Urinary Obstruction Due to Triplelennamine Hydrochloride. Wolfson, S. A.: J. A. M. A. **140**: 958, 1949.

A fifty-four-year-old male, who had been taking Pyribenzamine for a mild dermatitis, suddenly developed a painless urinary obstruction. Urinal-

ysis was normal. When Pyribenzamine was discontinued, the obstruction promptly abated. A subsequent trial with the drug reproduced the symptoms. Cardiospasm has been observed in human beings, and investigations carried out on the dog intestine and uterus have demonstrated the presence of spasmogenic properties in Pyribenzamine and other antihistaminics. It seems likely that the urinary symptoms in this case were the result of the spasmogenic property of Pyribenzamine. F.

Miscellaneous

Studies on the Mechanism of the Shwartzman Phenomenon. Thomas, L., and Stetson, C. A.: J. Exper. Med. **89**: 461, 1949.

Either meningococcal toxin or polysaccharide toxin from *Serratia marcescens* was injected intracutaneously in rabbits. Eighteen hours later the animals were killed and skin strips removed for study of tissue respiration. The respiratory quotient of skin from "prepared" rabbits tended to be higher than that of uninjected animals. This effect was more pronounced when the glucose concentration was increased. The increased carbon dioxide output of "prepared" skin was found to be due to aerobic glycolysis with formation and accumulation of lactic acid, both in vitro and in vivo. Prepared skin sites contained up to five times as much lactic acid as normal skin. This phenomenon could not be reproduced in vitro by adding bacterial toxin to normal skin samples, nor in vivo by such local irritants as undiluted human and horse serum, one per cent egg albumin, and streptococcal filtrate. Anaerobic glycolysis was also consistently higher in Shwartzman-prepared skin, but to a lesser degree.

The response of normal rabbit skin to the intracutaneous injection of known proteolytic enzymes was compared with the response in rabbits which had been given an intravenous injection of bacterial toxin. Papain failed to induce hemorrhagic lesions in normal skin but caused gross hemorrhagic lesions in injected animals. Crystalline trypsin, on the other hand, induced similar lesions in both experimental and control rabbits.

The mechanism of the Shwartzman phenomenon is tentatively described as follows: Bacterial toxin brings about increased tissue-lactic acid formation, which creates a favorable environment for protease. The intravenous injection of bacterial toxin decreases the effectiveness of the inhibitory mechanism for tissue protease, thus enabling this enzyme to act on tissue with resultant blood-vessel damage and hemorrhage. K.

Cardiac Lesions Produced in Rabbits by Massive Injections of Bovine Serum Gamma Globulin. More, R. H., Waugh, D., and Kobernick, S. D.: J. Exper. Med. **89**: 555, 1949.

Of seventeen rabbits subjected to two massive and one small intravenous dose of bovine serum gamma globulin, nine (52 per cent) developed focal granulomatous lesions in the heart valves and valve rings. Two animals developed lesions of the arteries of the heart, and in one instance necrosis of the arterial wall was observed. Control rabbits injected with saline failed to show such lesions. Detailed descriptions of the lesions and pictures are presented. The lesions were very similar but not identical to those seen in rheumatic fever in man. K.

Anatomic Observations in Fatal Cases of Bee and Wasp Stings. Wegelui, C.: Schweiz. med. Wehnschr. **78**: 1253, 1948.

Two fatal cases of bee sting and one fatal case of wasp sting are reported. Death resulted from a single sting in all three cases and occurred within one hour in two cases and within five days in the other case. In the latter case an extensive lobular pneumonia followed the initial unconsciousness and coma persisted until death. In all the cases nausea, cyanosis of the legs, vertigo, vomiting, pallor, and sweating were followed by coma. In one patient urticaria developed over the trunk. Postmortem findings included hyperemia of the internal organs, edema of the lungs and larynx, and petechial hemorrhages of the skin and mucous membranes. The pulmonary emphysema noted was regarded as suggestive of an allergic reaction. H.

Eosinophilia During Intensive Gold Therapy. Reisener, E. H., Jr., Lapin, L., and Steinbrocker, O.: New England J. Med. **240**: 881, 1949.

Serial hematologic observations made on eighteen patients undergoing intensive chrysotherapy revealed eosinophile counts from 5 to 45 per cent in all cases. The eosinophilia was not related to individual dosage, nor to the length of treatment. The groups receiving larger amounts of gold tended to show a higher mean eosinophile increase. There was no direct relationship between eosinophilia and the occurrence of toxic reactions. Marked eosinophilia is not a contraindication to further treatment. However, caution should be exercised when it occurs. H.

Diffuse Glomerulonephritis Produced in Rabbits by Massive Injections of Bovine Serum Gamma Globulin. More, R. H., and Waugh, D.: J. Exper. Med. **89**: 541, 1949.

Bovine serum gamma globulin, administered intravenously three times within twelve days to eighteen unilaterally nephrectomized rabbits, produced diffuse glomerulitis in fourteen of the animals. Five displayed moderate to severe renal lesions closely resembling those of human glomerulonephritis. Focal granulomata of the heart valves and valve rings and coronary arteritis were also observed. Precipitins for bovine serum albumin were present in all animals. In two animals that developed precipitins against their own kidneys eleven days after the first globulin injection, one had severe glomerulitis and the other pyelonephritis. Three animals showed precipitins to a pooled kidney extract at eleven days. Precipitins for rabbit, kidney, or liver extract were not demonstrable in any of the sera one week after the second large dose of globulin or nineteen days after the initial injection. Ten animals injected with saline served as controls. Coagulation time sometimes decreased for one week following the initial massive injection, but this did not recur following a second large dose. A transient prolongation of clotting time was noted eleven days after a small initial intravenous injection of globulin. K.

Neohetramine and Thephorin: Two New Antihistaminic Drugs. Aaron, T. H., and Criep, L. H.: Canad. M. A. J. **59**: 438, 1948.

The results of animal experimentation in vivo and in vitro with antihistaminic drugs are briefly reviewed. Toxicity studies were carried out on thirty-seven patients given 300 mg. per day of Thephorin for four days, and on seventeen patients given 300 mg. per day of Neohetramine for four days. In two patients, each of whom had arteriosclerotic heart disease, Thephorin

caused inversion of the T wave of the electrocardiogram. When the drug was discontinued the T wave became upright. None of the other patients showed electrocardiographic changes or alteration in the blood count, blood pressure, or urinalyses. A sporadic increase in activity was found in the electroencephalographic patterns of eight patients taking various antihistaminic drugs. Side reactions were encountered in 23 per cent of the patients taking Thephorin, 25 mg. "every four hours as needed," and in 10 per cent of patients taking one 50 mg. tablet of Neohetramine in the same manner.

K.

The Pertussis Agglutinogen Skin Test. Miller, J. J., Ryan, M. L., and Havard, E.: Am. J. Dis. Child. **75**: 872, 1948.

A delayed type of skin reaction, following an intracutaneous injection in children of acid-extracted material from *Hemophilus pertussis* organisms, indicates immunity to whooping cough as evidenced by the serum agglutinin titer. A negative cutaneous response, however, may coexist with a high serum agglutinin titer. The absence of skin hypersensitivity is, therefore, not necessarily an index of susceptability. Immunization of one hundred children with *H. pertussis* vaccine induced cutaneous hypersensitivity in 79 per cent. Cutaneous reactivity one year following vaccination was present in twenty-five of forty-three children who had received a total dose of eighty billion cells or more, and in only one of eleven children who received smaller doses. Cutaneous hypersensitivity persisted unabated for four years after vaccination and then declined. The serum agglutinin titer decreased during the first four years and a sharper rate of decrease occurred after this time. The skin test itself produced an increase in serum agglutinin titer within a week but subcutaneous injection of twenty billion organisms in saline was "far more effective."

Skin tests and agglutinative titers were studied on ten children with a past history of pertussis. Only one child showed a clear-cut positive cutaneous reaction. Agglutinative titers were low or not detectable in all, except in one instance where a child had previously received one dose of vaccine. It is suggested that the immunity conferred by an attack of pertussis is, for the most part, localized in the respiratory tract.

K.

Antihistaminic Drug Treatment of Acute Nephritis. Craig, J., Clark, N. S., and Chalmers, J. D.: Brit. M. J. **1**: 6, 1949.

The concept that acute nephritis may be an allergic response to bacterial toxins is discussed. Eight cases were treated with Neoantergan and their course was compared with that of nine consecutive cases of acute nephritis treated routinely in the hospital during the same period. The duration of activity, as measured by the presence of abnormal urinary findings was notably shorter in those patients receiving the antihistaminic drug. However, since acute nephritis is a disease which may run a variable course, no final evaluation of this treatment could be made on the basis of so small a number of cases.

H.